

Amendments to the Claims:

1. (Currently amended) A method of screening for an agent having efficacy in treating insulin resistance, the method comprising:

a) providing

i) a first biological sample obtained from an untreated insulin resistant subject,

ii) a second biological sample obtained from a subject who is normal or ~~comparatively~~ insulin-sensitive subject in comparison to said untreated insulin resistant subject;

iii) a third biological sample obtained from an insulin resistant subject who has been treated with a known treatment or compound which alters insulin sensitivity, and

iv) a fourth biological sample obtained from a subject who is normal or ~~comparatively~~ insulin-sensitive subject in comparison to said untreated insulin resistant subject and who has been treated with said known treatment or compound;

b) identifying at least one differentially expressed protein which is:

(i) differentially expressed in said first and second biological samples;

(ii) differentially expressed in said first and third biological samples; and

(iii) not differentially expressed in said second and fourth biological samples; or differentially expressed in said second and fourth biological samples to a lesser degree than in said first and third biological samples;

c) providing a fifth biological sample comprising cellular tissue susceptible to insulin action or a subcellular fraction thereof obtained from an insulin resistant subject,

wherein said fifth biological sample has been treated with said agent or said insulin resistant subject has been treated with said agent; ~~and~~

d) determining the effect of said agent on the level of expression of said at least one differentially expressed protein in said fifth biological sample; and

e) identifying an agents which alters the expression level towards that observed in the second or third biological sample as an agent having efficacy for the treatment of insulin resistance.

2. (Previously presented) The method of claim 1, wherein the agent is selected if it changes the expression of the at least one differentially expressed protein towards that of a normal subject or a more insulin sensitive subject.

3. (Previously presented) The method of claim 2, wherein the agent is selected if it converts the expression of the at least one differentially expressed protein to that of a normal or more insulin sensitive subject.

4. (Canceled)

5. (Previously presented) The method of claim 1, wherein the normal or comparatively insulin-sensitive subject of step a) is a normal subject or an abnormally insulin sensitive subject.

6. (Previously presented) The method of claim 5, wherein the abnormally insulin sensitive subject has acquired higher than normal sensitivity by exercise.

7. (Previously presented) The method of claim 1, wherein the cellular tissue of the fifth biological sample is selected

from the group consisting of liver, skeletal muscle, white or brown adipose tissue.

8-13. (Canceled)

14. (Previously presented) The method of claim 1, wherein the insulin-resistant subject of step a) is an animal which is insulin-resistant as a result of genetic mutation, and the normal or comparatively insulin-sensitive subject is a normal control animal.

15. (Previously presented) The method of claim 14, wherein the normal control animal is an insulin sensitive littermate of the genetically mutated animal.

16. (Previously presented) The method of claim 1, wherein the insulin-resistant subject of step a) is an animal which is insulin-resistant as a result of diet, and the normal or comparatively insulin-sensitive subject is a normal control animal.

17. (Previously presented) The method of claim 1, wherein the normal and insulin resistant subjects of step a) are animals which are insulin-sensitive on a natural diet, but develop insulin resistance when given an unnatural, laboratory diet.

18. (Previously presented) The method of claim 1, wherein the treatment which alters the level of insulin sensitivity comprises administration of an insulin-sensitizing drug.

19. (Original) The method of claim 18, wherein the insulin sensitizing drug is thiazolidinedione.

20. (Original) The method of claim 19, wherein the thiazolidinedione is rosiglitazone (BRL 49653).

21. (Original) The method of claim 18, wherein the insulin sensitizing drug is a non-thiazolidinedione which is (a) an agonist or partial agonist of the PPAR gamma nuclear receptor, (b) a b3-adrenoceptor agonist or (c) a leptin or leptin fragment.

22. (Previously presented) The method of claim 1, wherein the treatment which alters the level of insulin sensitivity comprises dietary restriction and/or exercise.

23. (Previously presented) The method of claim 1, wherein the fifth biological sample of step c) is taken from a subject suffering from non-insulin dependent diabetes.

24. (Previously presented) The method of claim 1, wherein the fifth biological sample of step c) is taken from a subject suffering from polycystic ovary syndrome, syndrome X, insulin resistance syndrome or type I diabetes.

25. (Currently amended) The method of claim 1, wherein the differentially expressed proteins are identified by two-dimensional gel electrophoresis.

26. (Canceled)

27. (Previously presented) The method of claim 1, further comprising the step of isolating at least one of the differentially expressed proteins identified in the method.

28. (Original) The method of claim 27, further comprising the step of characterizing the isolated protein.

29. (Canceled)

30. (Previously presented) The method of claim 28, further comprising identifying specific binding partners of the isolated protein.

31. (Previously presented) The method of claim 28, further comprising screening for agonists or antagonists of the isolated protein.

32. (Previously amended) The method of claim 1, wherein the agents or proteins are screened using a high throughput screening method.

33. (Previously presented) The method of claim 1 further comprising preparation of pharmaceutical composition comprising the identified agent, said method further comprising a) manufacturing the agent and b) formulating the agent with an acceptable carrier.

34-51. (Cancelled)

52. (Previously presented) The method of claim 1, wherein said biological samples are tissue samples or body fluid samples said method further comprising the steps of:

f) predicting the most appropriate and effective therapy to alleviate insulin resistance; and

g) monitoring the success of said therapy.

53. (Previously presented) The method of claim 1, wherein the comparatively insulin sensitive subject is a normal subject or an abnormally insulin sensitive subject.